REMARKS

Claims 34-51 and 54-61, as amended, appear in this application for the Examiner's review and consideration. Claim 34 has been amended for calrity. In particular, claim 34 has been amended to recite that the drug reservoir layer is a matrix of a hydrophilic polymer, support for which can be found in paragraph [0025] of the published application. Claim 34 has been further amended to recite that achieving the therapeutic concentration of the peptide, polypeptide or protein in the subject's blood for at least 6 hours is based on the delivery of the peptide, polypeptide or protein solely by diffusion from the patch through the micro-channels into the blood, support for which can be found in paragraph [0017] of the published application. As no new matter has been introduced by any of these changes and additions, their entry at this time is warranted.

Claim Rejections – 35 USC § 103

Claims 34-51 and 54 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,148,232 to Avrahami (referred to hereafter as "Avrahami"), in view of U.S. Patent No. 6,275,728 to Venkatraman et al. (referred to hereafter as "Venkatraman") in view of U.S. Patent No. 5,983,130 to Phipps et al. (referred to hereafter as "Phipps") in view of U.S. Patent No. 5,418,222 to Song et al. (referred to hereafter as "Song") in view of U.S. Patent No. 5,158,537 to Haak et al. (referred to hereafter as "Haak") in view of U.S. Patent No. 5,906,830 to Farinas et al. (referred to hereafter as "Farinas"). The Office Action states that Avrahami discloses a device that can create micro-channels, then be removed from the skin, and then a commercially available skin patch can be placed over the skin with the micro-channels. The Office Action further states that while Avrahami does not disclose particular skin patches, numerous patents describe electroporation devices and transdermal delivery devices including sustained release transdermal delivery devices. For example, Song discloses single and multiple layer collagen films for sustained release delivery of pharmaceuticals. Venkatraman discloses a hydratable drug reservoir film for electrotransport drug delivery devices. Phipps discloses an electrotransport agent delivery device for delivering a therapeutic agent through a body surface. Farinas discloses transdermal drug delivery systems comprising drug reservoirs wherein polymeric materials which are suitable for such devices include getalin and carrageenan. The Office Action states that it would have been obvious to take the motivational teaching of

Avrahami to perform electroporation of the skin followed by placement of a sustained delivery transdermal patch on the electroporated area of the skin.

Applicant respectfully disagrees with the characterization of the prior art. Avrahami does disclose a device for generating micro-channels in the stratum corneum of the skin, and that device is then removed from the skin in order to enhance the transdermal delivery of a substance that is subsequently placed on the skin. Avrahami utilizes a commercially available skin patch to supply the substance to be delivered. It should be emphasized, however, that skin patches for peptides, polypeptides or proteins were not commercially available at the filing date of the present application and such patches are not commercially available at present. This is due to the fact that transdermal delivery through intact skin from a patch of peptides, polypeptides or proteins is known to skilled artisans to be negligible. A skilled artisan would expect to achieve even less delivery if the peptide, polypeptide or protein is embedded in a polymeric matrix in the patch. Thus, to applicants' knowledge, no one has previously made such a product, commercially or otherwise, as it would not be expected to be a useful product.

None of the secondary references cited in the Office Action remedy the deficiencies of Avrahami. Venkatraman, Phipps, and Haak disclose electrotransport drug delivery devices which require application of electrical energy to the drug composition so as to iontophoretically deliver the drug into the subject's body. Song discloses single and multiple layer collagen films useful for wound dressing, but NOT for transdermal delivery. Farinas discloses a manufacturing method for preparing supersaturated drug reservoirs wherein the polymeric material useful to form the drug-polymer admixture is heated to a temperature that dissolves the drug in the polymer. The drug in Farinas is NOT a peptide, polypeptide or protein as heating of such agents to the melting temperature of the drug-polymer (e.g., 109°C or even to 140 °C as exemplified in Example 2 of Farinas) would denature the protein and consequently would destroy its activity, a totally undesired end result for the present invention. Thus, none of the references cited teaches or suggests that a peptide, polypeptide or a protein can be delivered through a region of the skin where micro-channels have been generated from a patch which comprises a drug reservoir layer which is a matrix of a hydrophilic polymer and a pharmaceutical composition comprising said agents so as to achieve a therapeutic blood concentration of said agents for extended period of time. Moreover, even if one of skilled in the art combines Avrahami and the references cited, he or she would not obtain the method as recited in claim 34 as amended.

In reference to specific comments made in the office action, Applicant resopnds as follows:

The statement that "Whether Avrahami utilizes a commercially available skin patch is irrelevant to the claim..." (section 4 of the Office Action). Applicant respectfully disagrees. The type of the skin patch is critical and very relevant to the method recited in claim 34 because the combination of generating micro-channels in the skin of a subject and affixing the specific patch which comprises a drug reservoir layer which is a matrix of a hydrophilic polymer and a pharmaceutical composition comprising a peptide, polypeptide or protein, such combination enables achieving sustained transdermal delivery of the peptide, polypeptide or protein.

The allegation that paragraphs [0017] and [0059] of the published application do not provide support for a method whereby passage of peptides, polypeptides or proteins occur by diffusion only (section 5 of the Office Action) is respectfully traversed. Paragraph [0017] of the published application clearly discloses that the active agent released from the drug reservoir layer of the patch simply moves through the micro-channels to the systemic circulation. No electrical energy is applied to the patch so as to iontophoretically deliver the active agent.

With reference to section 6, the Office Action suggests that the claim is not so narrow to be limited to diffusion only. As explained herein, the delivery of the peptide, polypeptide or protein from the patch into the skin is by diffusion only and claim 34 has been amended accordingly to make sure that there is no confusion on this point.

With reference to section 7, the statement in the Office Action that Song is not limited to wound, burn or trauma is incorrect. Song only discloses drug delivery to wound, burn or trauma sites only (col. 2, lines 50-60 and col. 6, lines 19-36 of Song). There is no indication in Song for transdermal delivery of a drug or for delivery of a drug to the skin. A skilled artisan would not look to Song for a teaching for applying a drug to intact skin but instead for assistance in treating damaged skin.

With reference to section 9, the allegation that Farinas provides a number of polymeric matrices, including those claimed by Applicants, is also incorrect. Farinas discloses hydrophobic polymers or alternatively a combination of hydrophobic and hydrophilic polymers for the drug reservoir. Farinas does not disclose or suggest a drug reservoir of a hydrophilic polymer. As a skiled artisan would appreciate, a drug reservoir of combinations of hydrophobic and hydrophilic polymers would not be a matrix of a hydrophilic polymer as claimed.

Furthermore, Farinas does not disclose nor suggest the use of active agents of peptides, polypeptides or proteins. The amended claims further distinguish the present method from Farinas, in that claim 34 now recites the drug reservoir is a matrix of a hydrophilic polymer and that the active agents are peptides, polypeptides or proteins, active agents that would not be considered as beign useful in patches that are applied to intact skin.

With reference to section 10, the method claim has been amended to recite that achieving the therapeutic concentration of the peptide, polypeptide or protein is based on the delivery of said peptide, polypeptide or protein by diffusion only from the patch through the micro-channels in the subject's skin and into the blood. Thus, Applicants submit that the amended claim is not open to other forms of administration, or to pateches of other materials or active agents.

With reference to section 15, Applicant notes that in contrary to the assertions in the Office Action, Song does not refer to iontophoresis in col. 3, lines 37-42 and does not disclose delivery of insulin and hGH for transdermal electrotransport delivery of peptides and polypeptides in col. 13, 39-50. As indicated herein above, Song does not teach transdermal delivery at all.

With reference to sections 20 and 21, the Office Action asserted that it would have been obvious to one of ordinary skill in the art to combine the teachings of Avrahami and Venkatraman to arrive at the invention of claim 34. This assertion is incorrect. As indicated herein above and in detail in the Amendment filed on May 31, 2011, Venkatraman discloses electrotransport delivery devices wherein the delivery of peptides, polypeptides or proteins is achieved by iontophoresis, namely by electrical energy. In contrast, the delivery of the peptide, polypeptide or protein in claim 34 is by diffusion only from the patch through the micro-channels to the blood (see paragraph [0017] of the published application).

With reference to section 22, Applicants repeat the comments made hereinabove with reference to section 15.

With reference to section 23, Haak discloses an iontophoretic delivery device which is different and distinguishable from the method recited in claim 34.

In view of the above, it is respectfully submitted that all current rejections have been overcome and should be withdrawn. Accordingly, the entire application is believed to be in condition for allowance, early notice of which would be appreciated.

Respectfully submitted,

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